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DICTIONARY FILE UPDATES: 7 MAR 2003 HIGHEST RN 497212-14-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

L1 545 CC,(2)C,(3,7)CJSQSP  
L2 2GCCS1PPCALNNPDCISQSP

FILE 'CA' ENTERED AT 07:44:57 ON 09 MAR 2003 COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

L3 208 L1  
L4 89 L1 AND CONOTOXIN  
L5 4 L2

L4 ANSWER 1 OF 89 CA COPYRIGHT 2003 ACS  
T1 Identification of the nicotinic receptor subtypes expressed on dopaminergic terminals in the rat striatum

L4 ANSWER 2 OF 89 CA COPYRIGHT 2003 ACS  
T1 Declines in different .beta.2\* nicotinic receptor populations in monkey striatum after nigrostriatal damage

L4 ANSWER 3 OF 89 CA COPYRIGHT 2003 ACS  
T1 .alpha.-\*\*\*Conotoxin\*\*\* IC from *Conus geographus*, a Novel Peptide Antagonist of Nicotinic Acetylcholine Receptors

L4 ANSWER 4 OF 89 CA COPYRIGHT 2003 ACS  
T1 The synthesis and structure of an n-terminal dodecanoic acid conjugate of .alpha.-\*\*\*conotoxin\*\*\*

L4 ANSWER 5 OF 89 CA COPYRIGHT 2003 ACS  
T1 Characterization of [125]epibatidine binding and nicotinic agonist-mediated 86Rb+ efflux in interpeduncular nucleus and inferior colliculus of .beta.2 null mutant mice

L4 ANSWER 6 OF 89 CA COPYRIGHT 2003 ACS  
T1 Toxins R Us: more pharmacological tools from nature's superstore

L4 ANSWER 7 OF 89 CA COPYRIGHT 2003 ACS  
T1 Alpha \*\*\*conotoxin\*\*\* peptides with analgesic properties

L4 ANSWER 8 OF 89 CA COPYRIGHT 2003 ACS  
T1 Differential nicotinic receptor expression in monkey basal ganglia: Effects of nigrostriatal damage

L4 ANSWER 9 OF 89 CA COPYRIGHT 2003 ACS  
T1 Methylcycaptonine is a potent antagonist of .alpha.-\*\*\*conotoxin\*\*\* -M1-sensitive presynaptic nicotinic acetylcholine receptors in rat striatum

L4 ANSWER 10 OF 89 CA COPYRIGHT 2003 ACS  
T1 Novel conotoxins for use in the therapeutic regulation of ion channel function

L4 ANSWER 11 OF 89 CA COPYRIGHT 2003 ACS  
T1 A novel choline-sensitive nicotinic receptor subtype that mediates enhanced GABA release in the chick ventral lateral geniculate nucleus

L4 ANSWER 12 OF 89 CA COPYRIGHT 2003 ACS  
T1 5-iodo-A-85-360 binds to .alpha.-\*\*\*conotoxin\*\*\* M1-sensitive nicotinic acetylcholine receptors (nAChRs) as well as alpha.4.beta.2\* subtypes

L4 ANSWER 13 OF 89 CA COPYRIGHT 2003 ACS  
T1 Involvement of the .alpha.3 subunit in central nicotinic binding populations

L4 ANSWER 14 OF 89 CA COPYRIGHT 2003 ACS  
T1 Solution conformation of .alpha.-\*\*\*Conotoxin\*\*\* El, a neuromuscular toxin specific for the .alpha.1/.delta.1 subunit interface of *Torpedo* nicotinic acetylcholine receptor

L4 ANSWER 15 OF 89 CA COPYRIGHT 2003 ACS  
T1 Protein sequences of synthetic *Conus* .alpha.-conotoxins and the therapeutic uses thereof as neuromuscular blocking agent

L4 ANSWER 16 OF 89 CA COPYRIGHT 2003 ACS

T1 New members of the mu.-\*\*\*conotoxin\*\*\* family for use in the treatment of disease associated with sodium channel function and cDNAs encoding them

L4 ANSWER 17 OF 89 CA COPYRIGHT 2003 ACS  
T1 Loss of nicotinic receptors in monkey striatum after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine treatment is due to a decline in .alpha.-\*\*\*conotoxin\*\*\*

L4 ANSWER 18 OF 89 CA COPYRIGHT 2003 ACS  
T1 Two new classes of conopeptides inhibit the alpha.1-adrenoceptor and noradrenaline transporter

L4 ANSWER 19 OF 89 CA COPYRIGHT 2003 ACS  
T1 Vulnerability of 125I-.alpha.-\*\*\*conotoxin\*\*\* M1 binding sites to nigrostriatal damage in monkey

L4 ANSWER 20 OF 89 CA COPYRIGHT 2003 ACS  
T1 Mechanisms for evolving hypervariability: the case of conopeptides

L4 ANSWER 21 OF 89 CA COPYRIGHT 2003 ACS  
T1 An efficient synthetic scheme for natural .alpha.-conotoxins and their analogues

L4 ANSWER 22 OF 89 CA COPYRIGHT 2003 ACS  
T1 An alpha.4.beta.4 nicotinic receptor subtype is present in chick retina: identification, characterization and pharmacological comparison with the transfected .alpha.4.beta.4 and .alpha.6.beta.4 subtypes

L4 ANSWER 23 OF 89 CA COPYRIGHT 2003 ACS  
T1 Structure-Activity Relationships in a Peptidic .alpha.7 Nicotinic Acetylcholine Receptor Antagonist

L4 ANSWER 24 OF 89 CA COPYRIGHT 2003 ACS  
T1 Protein and cDNA sequences of *Conus* conotoxins and therapeutic uses thereof

L4 ANSWER 25 OF 89 CA COPYRIGHT 2003 ACS  
T1 Alpha-conotoxins and nucleic acids encoding them

L4 ANSWER 26 OF 89 CA COPYRIGHT 2003 ACS  
T1 Protein and cDNA sequences of *Conus* .alpha.-conotoxins and the therapeutic uses thereof as neuromuscular blocking agent

L4 ANSWER 27 OF 89 CA COPYRIGHT 2003 ACS  
T1 125I-.alpha.-\*\*\*conotoxin\*\*\* M1 identifies a novel nicotinic acetylcholine receptor population in mouse brain

L4 ANSWER 28 OF 89 CA COPYRIGHT 2003 ACS  
T1 .beta.3 Subunit is present in different nicotinic receptor subtypes in chick retina

L4 ANSWER 29 OF 89 CA COPYRIGHT 2003 ACS  
T1 *Conus* peptides: novel probes for nicotinic acetylcholine receptor structure and function

L4 ANSWER 30 OF 89 CA COPYRIGHT 2003 ACS  
T1 UB-155: A novel nicotinic agonist with subtype selectivity implicates the .alpha.4.beta.2\* subtype in the modulation of dopamine release from rat striatal synaptosomes

L4 ANSWER 31 OF 89 CA COPYRIGHT 2003 ACS  
T1 Leu10 of .alpha.-\*\*\*conotoxin\*\*\* PhIB confers potency for neuronal nicotinic responses in bovine chromaffin cells

L4 ANSWER 32 OF 89 CA COPYRIGHT 2003 ACS  
T1 .rho.-\*\*\*Conotoxin\*\*\* peptides with .alpha.1-adrenoceptor antagonist activity, nucleic acids encoding them, antibodies, and therapeutic uses

L4 ANSWER 33 OF 89 CA COPYRIGHT 2003 ACS  
T1 Pairwise interactions between neuronal .alpha.7 acetylcholine receptors and .alpha.-\*\*\*conotoxin\*\*\* PhIB

L4 ANSWER 34 OF 89 CA COPYRIGHT 2003 ACS  
T1 Preparation of cyclized \*\*\*conotoxin\*\*\* peptides

L4 ANSWER 35 OF 89 CA COPYRIGHT 2003 ACS  
T1 Pharmacological characterization of the response of the leech pharynx to acetylcholine

L4 ANSWER 36 OF 89 CA COPYRIGHT 2003 ACS  
T1 Single amino acid substitutions in .alpha.-\*\*\*conotoxin\*\*\* PhIB shift selectivity for subtypes of the mammalian neuronal nicotinic acetylcholine receptor

L4 ANSWER 37 OF 89 CA COPYRIGHT 2003 ACS  
T1 Conopeptides from *Conus* striatus and *Conus* textile by cDNA cloning

L4 ANSWER 38 OF 89 CA COPYRIGHT 2003 ACS  
T1 Conopeptides from *Conus* striatus and *Conus* textile by cDNA cloning

L4 ANSWER 38 OF 89 CA COPYRIGHT 2003 ACS  
 TI Single-Residue Alteration in .alpha.- \*\*\*Conotoxin\*\*\*  
 TI Switches Its nAChR Subtype Selectivity PY 1999

L4 ANSWER 39 OF 89 CA COPYRIGHT 2003 ACS  
 TI Aromatic substitutions in .alpha.- \*\*\*conotoxin\*\*\* Iml. Synthesis of iodinated photoactivatable derivative PY 1999

L4 ANSWER 40 OF 89 CA COPYRIGHT 2003 ACS  
 TI Three-dimensional structure of alpha.- \*\*\*Conotoxin\*\*\* EI determined by <sup>1</sup>H NMR spectroscopy PY 1999

L4 ANSWER 41 OF 89 CA COPYRIGHT 2003 ACS  
 TI Minimal conformation of the .alpha.- \*\*\*conotoxin\*\*\* Iml for the .alpha.7 neuronal nicotinic acetylcholine receptor recognition: correlated CD, NMR and binding studies PY 1999

L4 ANSWER 42 OF 89 CA COPYRIGHT 2003 ACS  
 TI Functional .alpha.6-containing nicotinic receptors are present in chick retina PY 1999

L4 ANSWER 43 OF 89 CA COPYRIGHT 2003 ACS  
 TI Pairwise interactions between neuronal alpha.7 acetylcholine receptors and alpha.- \*\*\*conotoxin\*\*\* Iml PY 1999

L4 ANSWER 44 OF 89 CA COPYRIGHT 2003 ACS  
 TI Cloning and sequencing of alpha.- \*\*\*conotoxin\*\*\* sequences from *Conus textile* venom duct PY 1999

L4 ANSWER 45 OF 89 CA COPYRIGHT 2003 ACS  
 TI Solution structure of .alpha.- \*\*\*conotoxin\*\*\* Iml determined by two-dimensional NMR spectroscopy PY 1999

L4 ANSWER 46 OF 89 CA COPYRIGHT 2003 ACS  
 TI Solution Structure of .alpha.- \*\*\*Conotoxin\*\*\* Iml by <sup>1</sup>H Nuclear Magnetic Resonance PY 1999

L4 ANSWER 47 OF 89 CA COPYRIGHT 2003 ACS  
 TI Inhibition of nicotine-induced hippocampal norepinephrine release in rats by alpha-conotoxins MII and AIIIB microinjected into the locus caeruleus PY 1999

L4 ANSWER 48 OF 89 CA COPYRIGHT 2003 ACS  
 TI Uses of alpha.- \*\*\*conotoxin\*\*\* peptides PY 1999 1999 2001 2002

L4 ANSWER 49 OF 89 CA COPYRIGHT 2003 ACS  
 TI Identification of tyrosine sulfation in *Conus pennaceus* conotoxins .alpha.-PnIA and alpha.-PnIB: further investigation of labile sulfo- and phosphopeptides by electrospray, matrix-assisted laser desorption/ionization (MALDI) and atmospheric pressure MALDI mass spectrometry PY 1999

L4 ANSWER 50 OF 89 CA COPYRIGHT 2003 ACS  
 TI alpha.- \*\*\*Conotoxin\*\*\* Iml inhibits the .alpha.-bungarotoxin- resistant nicotinic response in bovine adrenal chromaffin cells PY 1999

L4 ANSWER 51 OF 89 CA COPYRIGHT 2003 ACS  
 TI NMR Solution Structure of alpha.- \*\*\*Conotoxin\*\* Iml and Comparison to Other Conotoxins Specific for Neuronal Nicotinic Acetylcholine Receptors PY 1999

L4 ANSWER 52 OF 89 CA COPYRIGHT 2003 ACS  
 TI Preparation and interaction of .alpha.- \*\*\*Conotoxin\*\*\* peptides with neuronal nicotinic acetylcholine receptors PY 1999 1999 1999 2000 2001

L4 ANSWER 53 OF 89 CA COPYRIGHT 2003 ACS  
 TI NMR spatial structure of .alpha.- \*\*\*conotoxin\*\*\* Iml reveals a common scaffold in small and snake toxins recognizing neuronal nicotinic acetylcholine receptors PY 1999

L4 ANSWER 54 OF 89 CA COPYRIGHT 2003 ACS  
 TI Accelerated chemical synthesis of peptides and small proteins PY 1999

L4 ANSWER 55 OF 89 CA COPYRIGHT 2003 ACS  
 TI Unmasking the functions of the chromaffin cell alpha.7 nicotinic receptor by using short pulses of acetylcholine and selective blockers PY 1998

L4 ANSWER 56 OF 89 CA COPYRIGHT 2003 ACS  
 TI .alpha.- \*\*\*Conotoxin\*\*\* AutB selectively blocks .alpha.3.beta.4 nicotinic acetylcholine receptors and nicotine-evoked norepinephrine release PY 1998

L4 ANSWER 57 OF 89 CA COPYRIGHT 2003 ACS  
 TI Three-Dimensional Solution Structure of alpha.- \*\*\*Conotoxin\*\*\* MII by NMR Spectroscopy: Effects of Solution Environment on Helicity PY 1998

L4 ANSWER 58 OF 89 CA COPYRIGHT 2003 ACS  
 TI Functional determinants by which snake and cone snail toxins block the .alpha.7 neuronal nicotinic acetylcholine receptors PY 1998

L4 ANSWER 59 OF 89 CA COPYRIGHT 2003 ACS  
 TI Molecular dissection of subunit interfaces in the nicotinic acetylcholine receptor PY 1998

L4 ANSWER 60 OF 89 CA COPYRIGHT 2003 ACS  
 TI Toxic conopeptides AIIA, AIIIB and AIIIC of cone snail venom active against nicotinic receptors PY 1998 1999 1998

L4 ANSWER 61 OF 89 CA COPYRIGHT 2003 ACS  
 TI Two distinct nicotinic receptors, one pharmacologically similar to the vertebrate .alpha.7-containing receptor, mediate Cl<sup>-</sup> currents in Aplysia neurons PY 1998

L4 ANSWER 62 OF 89 CA COPYRIGHT 2003 ACS  
 TI The 1.1.ANG Resolution Crystal Structure of [Tyr<sup>15</sup>]EpI, a Novel .alpha.- \*\*\*Conotoxin\*\*\* from *Conus episcopatus*. Solved by Direct Methods PY 1998

L4 ANSWER 63 OF 89 CA COPYRIGHT 2003 ACS  
 TI .alpha.- \*\*\*Conotoxin\*\*\* EpI, a novel sulfated peptide from *Conus episcopatus* that selectively targets neuronal nicotinic acetylcholine receptors PY 1998

L4 ANSWER 64 OF 89 CA COPYRIGHT 2003 ACS  
 TI Identification of residues in the neuronal .alpha.7 acetylcholine receptor that confer selectivity for \*\*\*conotoxin\*\*\* Iml PY 1998

L4 ANSWER 65 OF 89 CA COPYRIGHT 2003 ACS  
 TI Use of .alpha.- \*\*\*conotoxin\*\*\* MII? to treat disorders resulting from nicotine-stimulated dopamine release PY 1998 1998 1998 1998 1999

L4 ANSWER 66 OF 89 CA COPYRIGHT 2003 ACS  
 TI Structural elements in .alpha.- \*\*\*conotoxin\*\*\* Iml essential for binding to neuronal .alpha.7 receptors PY 1998

L4 ANSWER 67 OF 89 CA COPYRIGHT 2003 ACS  
 TI Use of \*\*\*conotoxin\*\*\* peptides Iml and MII as cardiovascular agents PY 1998 1998 2001 1999 2001

L4 ANSWER 68 OF 89 CA COPYRIGHT 2003 ACS  
 TI Differential inhibition by .alpha.- \*\*\*conotoxin\*\*\* -MII of the nicotinic stimulation of [<sup>3</sup>H] dopamine release from rat striatal synaptosomes and slices PY 1998

L4 ANSWER 69 OF 89 CA COPYRIGHT 2003 ACS  
 TI Three-Dimensional Solution Structure of alpha.- \*\*\*Conotoxin\*\*\* MII, an .alpha.3.beta.2 Neuronal Nicotinic Acetylcholine Receptor-Targeted Ligand PY 1997

L4 ANSWER 70 OF 89 CA COPYRIGHT 2003 ACS  
 TI Crystal Structure at 1.1.ANG. Resolution of .alpha.- \*\*\*Conotoxin\*\*\* PnIB: Comparison with .alpha.-Conotoxins PnIA and GII PY 1997

L4 ANSWER 71 OF 89 CA COPYRIGHT 2003 ACS  
 TI Determinants of specificity for .alpha.- \*\*\*conotoxin\*\*\* MII on .alpha.3.beta.2 neuronal nicotinic receptors PY 1997

L4 ANSWER 72 OF 89 CA COPYRIGHT 2003 ACS  
 TI Differential block of nicotinic synapses on B versus C neurons in sympathetic ganglia of frog by .alpha.-conotoxins MII and Iml PY 1997

L4 ANSWER 73 OF 89 CA COPYRIGHT 2003 ACS  
 TI Identification of genes encoding A-lineage \*\*\*conotoxin\*\*\* peptides by FCR PY 1996 1995 1996

L4 ANSWER 74 OF 89 CA COPYRIGHT 2003 ACS  
 TI \*\*\*Conotoxin\*\*\* peptides PY 1997 1995 1995 1996 1996 1996 1998 1998 1999

L4 ANSWER 75 OF 89 CA COPYRIGHT 2003 ACS  
 TI Use of \*\*\*conotoxin\*\*\* peptides U02 and MII for treating or detecting small-cell lung carcinoma PY 1996 1997 1996 1998 1998 1998

L4 ANSWER 76 OF 89 CA COPYRIGHT 2003 ACS  
 TI .alpha.- \*\*\*Conotoxin\*\*\* -Iml: a competitive antagonist at .alpha.-bungarotoxin-sensitive neuronal nicotinic receptors in hippocampal neurons PY 1996

L4 ANSWER 77 OF 89 CA COPYRIGHT 2003 ACS  
 TI \*\*\*Conotoxin\*\*\* peptides PY 1995 1995 1995 1995 1995 1997 1996 2002 1998 2002 2002 1997 1996 1997 1997 1997

L4 ANSWER 78 OF 89 CA COPYRIGHT 2003 ACS  
 TI The 1.1.ANG. crystal structure of the neuronal acetylcholine receptor antagonist .alpha.- \*\*\*conotoxin\*\*\* PnIA from *Conus pennaceus* PY 1996

L4 ANSWER 29 OF 89 CA COPYRIGHT 2003 ACS  
 TI A new alpha-\*\*\*conotoxin\*\*\* which targets alpha.3 beta.2 nicotinic acetylcholine receptors PY 1996

L4 ANSWER 80 OF 89 CA COPYRIGHT 2003 ACS  
 TI alpha-\*\*\*Conotoxin\*\*\* Imperidilis inhibits nicotine-evoked hormone release and cell proliferation in human neuroendocrine carcinoma cells PY 1996

L4 ANSWER 81 OF 89 CA COPYRIGHT 2003 ACS  
 TI \*\*\*Conotoxin\*\*\* peptides of *Conus striatus* PY 1995 1996 1995 1997 1996 2002 1998 2002

L4 ANSWER 82 OF 89 CA COPYRIGHT 2003 ACS  
 TI alpha-\*\*\*Conotoxin\*\*\* E1, A New Nicotinic Acetylcholine Receptor Antagonist with Novel Selectivity PY 1995

L4 ANSWER 83 OF 89 CA COPYRIGHT 2003 ACS  
 TI alpha-\*\*\*Conotoxin\*\*\* Im1 exhibits subtype-specific nicotinic acetylcholine receptor blockade: preferential inhibition of homomeric alpha.7 and alpha.9 receptors PY 1995

L4 ANSWER 84 OF 89 CA COPYRIGHT 2003 ACS  
 TI .alpha.-Conotoxins selectively inhibit one of the two acetylcholine binding sites of nicotinic receptors PY 1995

L4 ANSWER 85 OF 89 CA COPYRIGHT 2003 ACS  
 TI Conotoxins having acetylcholine receptor binding properties and their use in receptors assays and pharmaceuticals PY 1995 1995 1995 1995 1995 1995 1995 1995

L4 ANSWER 86 OF 89 CA COPYRIGHT 2003 ACS  
 TI New Mollusk-Specific alpha-Conotoxins Block *Aplysia* Neuronal Acetylcholine Receptors PY 1994

L4 ANSWER 87 OF 89 CA COPYRIGHT 2003 ACS  
 TI A nicotinic acetylcholine receptor ligand of unique specificity, alpha-\*\*\*conotoxin\*\*\* Im1 PY 1994

L4 ANSWER 88 OF 89 CA COPYRIGHT 2003 ACS  
 TI Novel alpha- and omega-conotoxins and *Conus striatus* venom PY 1992

L4 ANSWER 89 OF 89 CA COPYRIGHT 2003 ACS  
 TI \*\*\*Conotoxin\*\*\* -related compounds PY 1985

L4 ANSWER 6 OF 89 CA COPYRIGHT 2003 ACS AN 137:332622 CA  
 TI Toxins 'R' Us; more pharmacological tools from nature's supersite  
 AU Harvey, Alan L.  
 CS Strathclyde Institute for Drug Research, Dept of Physiology and Pharmacology, University of Strathclyde, Glasgow, G4  
 QN, UK  
 SO Trends in Pharmacological Sciences (2002), 23(5), 201-203  
 PB Elsevier Science Ltd. DT Journal; General Review LA English  
 RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE

L4 ANSWER 25 OF 89 CA COPYRIGHT 2003 ACS AN 133:146232 CA  
 TI Alpha-conotoxins and nucleic acids encoding them  
 IN Watkins, Maren; Olivera, Baldomero M.; Hillyard, David R.; McIntosh, J. Michael; Jones, Robert M.  
 PA University of Utah Research Foundation, USA; Cognetix, Inc. SO PCT Int. Appl., 229 pp CODEN: PIIXD2  
 DT Patent LA English FAN:CNT 2  
 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2000044776 A1 20000803 WO 2000-US1979 20000128  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW, GH, GM, KE, LS, MW, SD, SI, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 147130 A1 2001024 EP 2000-908382 20000128  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO  
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 PRAJ US 1999-118381P P 19990129  
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 OS MARPAT 133:4632  
 RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE  
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L4 ANSWER 26 OF 89 CA COPYRIGHT 2003 ACS AN 133:131093 CA  
 TI Protein and cDNA sequences of *Conus*.alpha.-conotoxins and the therapeutic uses thereof as neuromuscular blocking agent  
 IN Olivera, Baldomero M.; Layer, Richard T.; Watkins, Maren; Hillyard, David R.; McIntosh, J. Michael; Jones, Robert M.  
 PA University of Utah Research Foundation, USA; Cognetix, Inc. SO PCT Int. Appl., 95 pp CODEN: PIIXD2  
 DT Patent LA English FAN:CNT 1  
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 RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 16 OF 89 CA COPYRIGHT 2003 ACS  
 AN 136:146437 CA  
 TI New members of the .mu.-\*\*\*conotoxin\*\*\* family for use in the treatment of disease associated with sodium channel function and cDNAs encoding them  
 IN Olivera, Baldomero M.; McIntosh, J. Michael; Garrett, James E.; Watkins, Maren; Cruz, Lourdes J.; Shon, Ki-Joon; Jacobsen, Richard; Jones, Robert M.; Carter, G. Edward; Shen, Gregory S.  
 PA University of Utah Research Foundation, USA; Cognetix, Inc. SO PCT Int. Appl., 231 pp CODEN: PIIXD2  
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 PRAJ US 2000-219619P P 20000721  
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L4 ANSWER 25 OF 89 CA COPYRIGHT 2003 ACS AN 133:146232 CA  
 TI Alpha-conotoxins and nucleic acids encoding them  
 IN Watkins, Maren; Olivera, Baldomero M.; Hillyard, David R.; McIntosh, J. Michael; Jones, Robert M.  
 PA University of Utah Research Foundation, USA; Cognetix, Inc. SO PCT Int. Appl., 229 pp CODEN: PIIXD2  
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L4 ANSWER 26 OF 89 CA COPYRIGHT 2003 ACS AN 133:131093 CA  
 TI Protein and cDNA sequences of *Conus*.alpha.-conotoxins and the therapeutic uses thereof as neuromuscular blocking agent  
 IN Olivera, Baldomero M.; Layer, Richard T.; Watkins, Maren; Hillyard, David R.; McIntosh, J. Michael; Jones, Robert M.  
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 DT Patent LA English FAN:CNT 1  
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PI WO 2000043409 A2 20000727 WO 2000-US1372 20000121  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM  
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 OS MARPAT 133:131093

L4 ANSWER 32 OF 89 CA COPYRIGHT 2003 ACS  
 AN 132:288791 CA  
 TI .mo- \*\*\*Conotoxin\*\*\* peptides with alpha-1-adrenoceptor antagonist activity, nucleic acids encoding them, antibodies, and therapeutic uses  
 IN Lewis, Richard James; Alewood, Paul Francis; Sharpe, Iain Andrew  
 PA The University of Queensland, Australia SO PCT Int. Appl., 47 pp. CODEN: PIXXD2  
 DT Patent LA English FAN,CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2000020443 A1 20000413 WO 1999-AU843 19991001  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM  
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 AU 9963211 A1 20000426 EP 1999-63211 19991001  
 AU 117681 A1 20010725 EP 1999-950405 19991001  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO  
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 PRAI AU 1998-5273 A 19981002  
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L4 ANSWER 34 OF 89 CA COPYRIGHT 2003 ACS AN 132:231373 CA  
 TI Preparation of cyclized \*\*\*conotoxin\*\*\* peptides  
 IN Craik, David James; Daly, Norelle Lee; Nielsen, Katherine Justine  
 PA University of Queensland, Australia SO PCT Int. Appl., 43 pp. CODEN: PIXXD2  
 DT Patent LA English FAN,CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2000015654 A1 20000323 WO 1999-AU769 19990914  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM  
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 AU 9960705 A1 20000403 AU 1999-60705 19990914  
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 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO  
 PRAI AU 1998-5895 A 19980914

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 RE,CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 52 OF 89 CA COPYRIGHT 2003 ACS AN 130:297009 CA  
 TI Preparation and interaction of alpha- \*\*\*conotoxin\*\*\* peptides with neuronal nicotinic acetylcholine receptors  
 IN Shon, Ki-joon; Olivera, Baldomero M.; Rivier, Jean E.; Koerber, Steven C.; Shen, Gregory S.; McIntosh, J. Michael; Cartier, G. Edward; Yoshikami, Doju  
 PA University of Utah Research Foundation, USA SO Case Western Reserve University; Salk Institute; Cognetix, Inc. SO PCT Int. Appl., 176 pp. CODEN: PIXXD2 DT Patent LA English FAN,CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9921878 A1 19990506 WO 1998-US22368 19981023  
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM  
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 BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
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 PRAI US 1997-62783P P 19971024  
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 OS MARPAT 130:297009  
 RE,CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD THE REFORMAT

L4 ANSWER 60 OF 89 CA COPYRIGHT 2003 ACS AN 130:21651 CA  
 TI Toxic conopeptides AuaA, AuaB and AuaC of cone snail venom active against nicotinic receptors  
 IN McIntosh, J. Michael; Cartier, G. Edward; Yoshikami, Doju; Luo, Sijin; Olivera, Baldomero M.  
 PA University of Utah Research Foundation, USA SO PCT Int. Appl., 22 pp. CODEN: PIXXD2 DT Patent LA English FAN,CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9851322 A1 19981119 WO 1998-US7004 19980409  
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
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 OS MARPAT 130:21651  
 E,CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD THE REFORMAT

L4 ANSWER 65 OF 89 CA COPYRIGHT 2003 ACS AN 129:37452 CA  
 TI Use of alpha- \*\*\*conotoxin\*\*\* MII to treat disorders resulting from nictoine-stimulated dopamine release  
 IN McIntosh, J. Michael; Kulak, Jennifer M.; Yoshikami, Doju; Olivera, Baldomero M.  
 PA University of Utah Research Foundation, USA SO PCT Int. Appl., 30 pp. CODEN: PIXXD2 DT Patent LA English FAN,CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9824462 A1 19980611 WO 1997-US22350 19971205

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RW, GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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PRAI US 1998-761674 19961206

WO 1997-US22350 19971205

RECNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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AU 695055 B2 19980806  
EP 844883 A1 19980603 EP 1996-921234 19960604  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
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PRAI US 1993-84848 A2 19930629  
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W: AU, CA, JP  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
US 5559872 A 19970121 US 1995-487174 19950607  
AU 9662503 A1 19961230 AU 1996-62503 19960604  
AU 695055 B2 19980806  
EP 844883 A1 19980603 EP 1996-921234 19960604  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
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PRAI US 1995-48714 A 19950607  
US 1993-84848 A2 19930629  
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PI WO 9640211 A1 19961219 WO 1996-US7962 19960604  
W: AU, CA, JP  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
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AU 9662503 A1 19961230 AU 1996-62503 19960604  
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
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PRAI US 1995-48714 A 19950607  
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PI US 55432155 A 19950711 US 1993-137800 19931019  
CA 2165566 AA 19950112 US 1993-84848 19930629  
CA 2172989 AA 19950427 CA 1994-2172989 19941019  
WO 951256 A1 19950427 WO 1994-US11927 19941019  
W: AU, CA, JP  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
AU 681216 B2 19970821 EP 1995-901691 19941019  
EP 728146 A1 19960828 EP 1995-901691 19941019  
B1 2020109  
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
JP 10509415 T2 19980914 JP 1994-512187 19941019  
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 US 5589340 A 19961231 US 1995-477383 19950607  
 US 5595972 A 19970121 US 1995-487174 19950607  
 US 5633347 A 19970527 US 1995-480750 19950607  
 AU 699078 A1 19971120 AU 1997-35197 19970821  
 AU 699078 B2 19981119 PRAI US 1993-84848 A2 19930629  
 US 1993-137800 A 19931019 WO 1994-US1927 W 19941019

L4 ANSWER 78 OF 89 CA COPYRIGHT 2003 ACS AN 124:335314 CA

TI The 1.1 ANG. crystal structure of the neuronal acetylcholine receptor antagonist, *alpha*.-\*\*\*conotoxin\*\*\*

penicatus

AU Hu, Shu-Hong; Gehrmann, John; Gudrat, Luke W.; Atwood, Paul F.; Craik, David J.; Martin, Jennifer L.

CS Center Drug Design and Development, Univ Queensland, St. Lucia, 4072, Australia

SO Structure (London) (1996), 6(4), 417-423 CODEN: STRUE6; ISSN: 0969-2126 PB Current Biology

DT Journal LA English

AB The 1.1 ANG. crystal structure of synthetic PhIA was detd. by direct methods using the Shake-and-Bake program. The three-dimensional structure incorporates a beta turn followed by two alpha-helical turns. The conformation is stabilized by two disulfide bridges that form the interior of the mol., with all other side chains oriented outwards. The compact architecture of the PhIA toxin provides a rigid framework for presentation of chem. groups that are required for activity. The structure is characterized by distinct hydrophobic and polar surfaces; a 16 ANG. segn. of the sole pos. and neg. charges (these two charged residues being located at opposite ends of the mol.) a hydrophobic region and a protruding tyrosine side chain. These features may be important for the specific interaction of PhIA with neuronal nAChR.

L4 ANSWER 81 OF 89 CA COPYRIGHT 2003 ACS AN 124:48165 CA

TI \*\*\*Conotoxin\*\*\* peptides of *Conus striatus*

IN Olivera, Baldomero M.; Cruz, Lourdes J.; Hilliard, David R.; McIntosh, J. Michael; Santos, Amenaufina D.

PA University of Utah Research Foundation, USA SO PCT Int. Appl., 66 pp. CODEN: PIIXD2

DT Patent LA English FAN,CNT7

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9511256 A1 19950427 WO 1994-US1927 19941019

W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 554774 A 19960507 US 1993-137800 19931019

AU 9510831 A1 19950508 AU 1995-10831 19941019

AU 681216 B2 19970821 EP 1995-901691 19941019

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

JP 10509415 T2 19980914 JP 1994-512487 19941019

AT 211764 E 20020115 AT 1995-901691 19941019

PRAI US 1993-137800 A 19931019 US 1993-84848 A2 19930629

US 1993-84848 A2 19930629

WO 1994-US1927 W 19941019

PI WO 9501436 A1 19950112 WO 1994-US7194 19940627

W: AU, CA, JP, KR RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5432155 A 19950711 US 1993-84848 19930629

CA 2165566 A 19950112 CA 1994-2165566 19940527

AU 9471158 A1 19950124 AU 1994-71158 19940527

AU 677837 B2 19970612 EP 706366 A1 19960417 EP 1994-920316 19940627

US 5700778 A 19971223 US 1995-456499 19950602

AU 97335197 A1 19971120 AU 1997-35197 19970821

AU 699078 B2 19981119 PRAI US 1993-84848 A 19930629

WO 1994-US7194 W 19940627

OS MARRAT 123:50449 AB Substantially pure conotoxins are provided which inhibit synaptic transmissions at the neuromuscular junctions and which are useful both in vivo and in assays because they specifically target particular receptors, such as the acetylcholine receptor, and acetylcholine receptors and in pharmaceuticals (no data). Thirteen different conotoxins config. 16-46 amino acids were prep'd. by solid phase peptide synthesis and tested for biol. activity.

L4 ANSWER 86 OF 89 CA COPYRIGHT 2003 ACS AN 124:201190 CA

TI New Mollusk-Specific *alpha*-Conotoxins Block Aplysia Neuronal Acetylcholine Receptors

AU Fainzilber, Michael; Hasson, Ark; Oren, Ruth; Buflingame, Alma L.; Gordon, Dalia; Spira, Michal E.; Zlotkin, Eiliahu

CS Sibleman Institute of Life Sciences, Hebrew University of Jerusalem, Jerusalem, 91904, Israel

SO Biochemistry (1994), 33(32), 9523-9 CODEN: BICHAW; ISSN: 0006-2960 DT: Journal LA English

AB Two mollusk-specific neurotoxic peptides from the venom of the molluscivorous snail *Conus penicatus* are described.

These new toxins block acetylcholine receptors (AChR) of cultured Aplysia neurons. Bath application of 0.5-1  $\mu$ M toxin

induces 5-10-mV membrane depolarization, which recovers to the control level within 1-3 min in the presence of the toxin. The response is blocked by 1 mM hexamethonium. Concomitantly with the transient depolarization, the toxins block approx. 90%

sequences of the toxins (*alpha*.-PhIA, GCGSLPPCAANPNDYC-NH2; *alpha*.-PhIB, GCGSLPPCALSNPDYC-NH2) enable their classification as novel *alpha*-conotoxins. The sequences differ from those of previously described *alpha*-conotoxins in a no. of features, the most striking of which is the presence of a single neg. charged residue in the C-terminal loop. This loop contains a pos. charged residue in piscivorous venom *alpha*-conotoxins. In contrast to other *alpha*-conotoxins, which are selective for vertebrate skeletal muscle nicotinic ACh receptors, these *Conus penicatus* toxins block neuronal ACh receptors in molluscs. As such they are new poisons which can be used to define subtypes of ACh receptors, and they should be useful tools in the study of structure-function relationships in ACh receptors.

AB We report the isolation and characterization of a novel nicotinic acetylcholine receptor (nAChR) ligand. The toxin is an 18 amino acid peptide and is the first reported *alpha*.-\*\*\*conotoxin\*\*\* from an Atlantic fish-hunting cone. The toxin was purified from the venom of *Conus emarginatus* and is called *alpha*.-\*\*\*conotoxin\*\*\*. The sequence diverges from that of previously isolated *alpha*.-conotoxins. We demonstrate that this structural divergence has functional consequences. In Torpedo nAChRs, *alpha*.-\*\*\*conotoxin\*\*\* EI selectively binds the agonist site near the *alpha*./*delta*. subunit interface in contrast to *alpha*.-\*\*\*conotoxin\*\*\* MI which selectively targets the *alpha*./*gamma*. ligand binding site. In mammalian nAChRs, *alpha*.-

AB *alpha*.-\*\*\*conotoxin\*\*\* EI shows high affinity for both the *alpha*./*delta*. and *alpha*./*gamma*. subunit interfaces (with some preference

for the *alpha*./*delta*. site), whereas *alpha*.-\*\*\*conotoxin\*\*\* MI is highly selective for the *alpha*./*delta*. ligand binding site. The sequence of the peptide is: Arg-Asp-Hyp-Cys-Cys-Tyr-His-Pro-Thr-Cys-Asn-Met-Ser-Asn-Pro-Gln-Ile-Cys-NH2, with disulfide bridging between Cys4-Cys10 and Cys5-Cys18, analogous to those of previously described *alpha*.-conotoxins. This sequence has been verified by total chem. synthesis. Thus, *alpha*.-\*\*\*conotoxin\*\*\* EI is a newly-available tool with unique structure and function for characterization of nAChRs.

L4 ANSWER 85 OF 89 CA COPYRIGHT 2003 ACS AN 123:50449 CA

TI Conotoxins having acetylcholine receptor binding properties and their use in receptors assays and pharmaceuticals

IN Olivera, Baldomero M.; Rivier, Jean E. F.; Cruz, Lourdes J.; Abagadie, Fe; Hopkins, Chris E.; Dykert, John; Torres, Josep L.

PA Salk Institute for Biological Studies, USA; University of Utah Research Foundation

SO PCT Int. Appl. 55 pp. CODEN: PIIXD2

DT Patent LA English FAN,CNT7

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9501436 A1 19950112 WO 1994-US7194 19940627

W: AU, CA, JP, KR RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

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AU 677837 B2 19970612 EP 706366 A1 19960417 EP 1994-920316 19940627

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AU 97335197 A1 19971120 AU 1997-35197 19970821

AU 699078 B2 19981119 PRAI US 1993-84848 A 19930629

WO 1994-US7194 W 19940627

OS MARRAT 123:50449 AB Substantially pure conotoxins are provided which inhibit synaptic transmissions at the neuromuscular junctions and which are useful both in vivo and in assays because they specifically target particular receptors, such as the acetylcholine receptor, and acetylcholine receptors and in pharmaceuticals (no data). Thirteen different conotoxins config. 16-46 amino acids were prep'd. by solid phase peptide synthesis and tested for biol. activity.

L4 ANSWER 86 OF 89 CA COPYRIGHT 2003 ACS AN 124:201190 CA

TI New Mollusk-Specific *alpha*-Conotoxins Block Aplysia Neuronal Acetylcholine Receptors

AU Fainzilber, Michael; Hasson, Ark; Oren, Ruth; Buflingame, Alma L.; Gordon, Dalia; Spira, Michal E.; Zlotkin, Eiliahu

CS Sibleman Institute of Life Sciences, Hebrew University of Jerusalem, Jerusalem, 91904, Israel

SO Biochemistry (1994), 33(32), 9523-9 CODEN: BICHAW; ISSN: 0006-2960 DT: Journal LA English

AB Two mollusk-specific neurotoxic peptides from the venom of the molluscivorous snail *Conus penicatus* are described.

These new toxins block acetylcholine receptors (AChR) of cultured Aplysia neurons. Bath application of 0.5-1  $\mu$ M toxin

induces 5-10-mV membrane depolarization, which recovers to the control level within 1-3 min in the presence of the toxin. The response is blocked by 1 mM hexamethonium. Concomitantly with the transient depolarization, the toxins block approx. 90%

sequences of the toxins (*alpha*.-PhIA, GCGSLPPCAANPNDYC-NH2; *alpha*.-PhIB, GCGSLPPCALSNPDYC-NH2) enable their classification as novel *alpha*-conotoxins. The sequences differ from those of previously described *alpha*-conotoxins in a no. of features, the most striking of which is the presence of a single neg. charged residue in the C-terminal loop. This loop contains a pos. charged residue in piscivorous venom *alpha*-conotoxins. In contrast to other *alpha*-conotoxins, which are selective for vertebrate skeletal muscle nicotinic ACh receptors, these *Conus penicatus* toxins block neuronal ACh receptors in molluscs. As such they are new poisons which can be used to define subtypes of ACh receptors, and they should be useful tools in the study of structure-function relationships in ACh receptors.

L4 ANSWER 82 OF 89 CA COPYRIGHT 2003 ACS AN 123:33053 CA

TI *alpha*.-\*\*\*Conotoxin\*\*\* EI, A New Nicotinic Acetylcholine Receptor Antagonist with Novel Selectivity

AU Martinez, Jennifer S.; Olivera, Baldomero M.; Gray, William R.; Craig, A.; Grey, Grobe, Duncan R.; Abramson, Stewart N.; McIntosh, J. Michael

SO Department of Biology, University of Utah, Salt Lake City, UT, 84112, USA

CS Biochemistry (1995), 34(44), 14519-26 CODEN: BICHAW; ISSN: 0006-2960 PB American Chemical Society

DT Journal LA English

AB We report the isolation and characterization of a novel nicotinic acetylcholine receptor (nAChR) ligand. The toxin is an 18 amino acid peptide and is the first reported *alpha*.-\*\*\*conotoxin\*\*\* from an Atlantic fish-hunting cone. The peptide was purified from the venom of *Conus emarginatus* and is called *alpha*.-\*\*\*conotoxin\*\*\*. The sequence diverges from that of previously isolated *alpha*.-conotoxins. We demonstrate that this structural divergence has functional consequences. In Torpedo nAChRs, *alpha*.-\*\*\*conotoxin\*\*\* EI selectively binds the agonist site near the *alpha*./*delta*. subunit interface in contrast to *alpha*.-\*\*\*conotoxin\*\*\* MI which selectively targets the *alpha*./*gamma*. ligand binding site. In mammalian nAChRs, *alpha*.-

AB *alpha*.-\*\*\*conotoxin\*\*\* EI shows high affinity for both the *alpha*./*delta*. and *alpha*./*gamma*. subunit interfaces (with some preference

for the *alpha*./*delta*. site), whereas *alpha*.-\*\*\*conotoxin\*\*\* MI is highly selective for the *alpha*./*delta*. ligand binding site. The sequence of the peptide is: Arg-Asp-Hyp-Cys-Cys-Tyr-His-Pro-Thr-Cys-Asn-Met-Ser-Asn-Pro-Gln-Ile-Cys-NH2, with disulfide bridging between Cys4-Cys10 and Cys5-Cys18, analogous to those of previously described *alpha*.-conotoxins. This sequence has been verified by total chem. synthesis. Thus, *alpha*.-\*\*\*conotoxin\*\*\* EI is a newly-available tool with unique structure and function for characterization of nAChRs.

L4 ANSWER 88 OF 89 CA COPYRIGHT 2003 ACS AN 117:206755 CA

TI Novel *alpha*.- and *omega*.-conotoxins and *Conus striatus* venom

AU Ramilo, Cecilia A.; Zafaralla, Glenn C.; Nadas, Laszlo; Hammerland, Lance G.; Yoshikami, Doju; Gray, William R.; Krishnan, Ramasharma; Ramachandran, J.; Willanich, George; et al.

CS Mar. Sci. Inst., Univ. Philippines, Quezon City, 1101, Philippines

SO Biochemistry (1992), 31(41), 9919-26 CODEN: BICHAW; ISSN: 0006-2960

DT Journal  
LA English  
AB Three neurotoxic peptides from the venom of *C. stratus* were purified, biochem. characterized, and chem. synthesized. One of these, an acetylcholine receptor blocker designated *alpha*-\*\*\*conotoxin\*\*\* SII, has the sequence GCCNIPACGPNVGCGTSCS. In contrast to all other *alpha*-conotoxins, SII has 3 disulfide bonds (instead of two), has no net pos. charge, and has a free C-terminus. The other 2 paralytic peptides are Ca channel-targeted *omega*-conotoxins, SVIA and SVIB. *omega*-SVIA is the smallest natural *omega*-\*\*\*conotoxin\*\*\* so far characterized and has the sequence CRSSGSPCGVTSICGRCYRGKCT-NH<sub>2</sub>. Although *omega*-\*\*\*conotoxin\*\*\* SVIA is a potent paralytic toxin in lower vertebrate species, it was much less effective in mammals. The third toxin, *omega*-\*\*\*conotoxin\*\*\* SVIB, has the sequence CKLKGQSCRKTSVDCSGSGSGKCNH<sub>2</sub>. This peptide has a different pharmac. specificity from other *omega*-conotoxins previously purified from *Conus* venoms; only *omega*-\*\*\*conotoxin\*\*\* SVIB has proven to be lethal to mice upon ic injection. Binding competition expts. with rat brain synaptosomal membranes indicate that the high-affinity binding site for *omega*-\*\*\*conotoxin\*\*\* SVIB is distinct from the high-affinity *omega*-\*\*\*conotoxin\*\*\* GVIA or MVIA site.

L4 ANSWER 89 OF 89 CA COPYRIGHT 2003 ACS AN 105:43332 CA

TI \*\*\*Conotoxin\*\*\*-related compounds

IN Sakakibara, Shunpei; Nishiochi, Yuji

PA Ajinomoto Co., Inc., Japan SO Jpn. Kokai Tokkyo Koho, 16 pp.

CODEN: JKXXAF DT Patent LA Japanese

FAN CNT<sup>1</sup> PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 60022899 A2 19851112 JP 1984-83463 19840425

PRAI JP 1984-83463 19840425

GI

/Structure 1 in file .gra/

AB The title compds. [U = Gly-A<sub>1</sub>-G<sub>1</sub>-H; V = Pro, Gly; W = NH<sub>2</sub>, OH], useful as muscle relaxants and hypnotics (effectiveness comparable to that of a tubocurarine deriv.), were prep'd. Thus, the protected cyclic oligopeptide amine II (Acn = AcNH<sub>2</sub>C<sub>12</sub>) was dissolved in aq. MeOH/iodoxane contg. HCl and 0.1N iodine/MeOH added with vigorous agitation. After 20 min the reaction was stopped by addn. of ascorbic acid in citric acid buffer (pH 5.0) to give 11% I (U = H, W = NH<sub>2</sub>, V = Pro).

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TI Pairwise interactions between neuronal *alpha*-7 acetylcholine receptors and *alpha*-conotoxin PnIB PY 2000

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TI Single amino acid substitutions in *alpha*-conotoxin PnIB shift selectivity for subtypes of the mammalian neuronal nicotinic acetylcholine receptor PY 1999

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TI Uses of alpha-conotoxin peptides PY 1999 1999 2001 2002

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TI Accelerated chemical synthesis of peptides and small proteins PY 1999

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AN 132:132466 CA

TI Single amino acid substitutions in *alpha*-conotoxin PnIB shift selectivity for subtypes of the mammalian neuronal nicotinic acetylcholine receptor

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AB The *alpha*-conotoxins, a class of nicotinic acetylcholine receptor (nAChR) antagonists, are emerging as important probes of the role played by different nAChR subtypes in cell function and communication. In this study, the native *alpha*-conotoxins PnIA and PnIB were found to cause conen.-dependent inhibition of the ACh-induced current in all rat parasympathetic neurons examined, with IC50 values of 14 and 33 nM, and a maximal iedi. in current amplitude of 87% and 71%, resp. The modified

alpha-conotoxin N11S<sup>1</sup>PnIA reduced the ACh-induced current with an IC50 value of 375 nM and a maximally effective conc. caused 91% block. [A10]PnIA was the most potent inhibitor, reducing the ACh-induced current in approx. 80% of neurons, with an IC50 value of 1.4 nM and 46% maximal block of the total current. The residual current was not inhibited further by alpha-bungarotoxin, but was further reduced by the *alpha*-conotoxins PnIA or PnIB, and by mecamylamine. 1H NMR studies indicate that PnIA, PnIB, and the analogs, [A10]PnIA and N11S<sup>1</sup>PnIA, have identical backbone structures. The authors propose that positions 10 and 11 of PnIA and PnIB influence potency and der. selectivity among *alpha*-7 and other nAChR subtypes, including *alpha*-3, *beta*-2 and *alpha*-3, *beta*-4. Four distinct components of the nicotinic ACh-induced current in mammalian parasympathetic neurons have been dissected with these conopeptides.

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